

clear, and exact terms as to enable any person skilled in the art to make and use the same and/or failed to particularly point out and distinctly claim the subject matter which applicants regarded as their invention. More specifically, process claim 1 as written did not define a variable X in it as found in Formula 1.

Applicants have amended claim 1, specifically step (b) thereof, to indicate that the compound of formula (II) is reacted with “a Lewis acid of structure  $PX_5$  where X is a halo group.” Support for this amendment can be found on page 5 of the subject specification, lines 25-27 where it is disclosed that “[s]uitable acids in said process of the invention for the conversion of compounds of formula (II) into compounds of formula (I) include Lewis Acids, such as phosphorus pentachloride or phosphorus pentabromide; preferably phosphorus pentachloride.”

Applicants believe that the above-noted amendment to the claim clarifies the source of X in the XH portion of the structure of formula (I) and accordingly overcomes the rejection of the claims under 35 U.S.C. §112, first and second paragraphs. Consequently, this rejection is respectfully requested to be withdrawn.

The Office Action next rejected claims 1-4, 7-15, 25, and 28-39 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,020,329 to Bateson et al. (hereinafter referred to as “Bateson et al.”). The rejection of the claims is grounded in the conclusion drawn by the Examiner that the p-nitrobenzyl or allyl group used by the present invention as the protecting agent are obvious in view of their alleged equivalence to the groups taught by Bateson et al. at column 3, lines 16-18 thereof. The Examiner went on to note in the Office Action that “[a]pplicants need to show that unexpected effects arise from the use of one protecting group rather than another.”

More particularly, the rejection of the claims made by the Examiner based on Bateson et al. relies on the alleged equivalence of the p-methoxybenzyl esters taught by Bateson et al. with the p-nitrobenzyl and allyl groups of the present invention. In response to this conclusion drawn by the Office Action, the applicants wish to respectfully point out that the p-nitrobenzyl group and the allyl group used in the present invention provide crystalline intermediates which allow for better isolation and purification across the whole synthesis than the p-methoxybenzyl esters of Bateson et al. In fact, applicants had tried other protecting groups only to result in non-crystalline intermediates and the need to use extensive chromatographic purifications in order to achieve acceptable quality.

In addition, it is noted that the p-nitrobenzyl group can be removed if needed with sodium dithionite under very mild conditions avoiding the use of hydrogenation conditions needed to remove other benzylic protecting groups like p-methoxybenzyl, which cannot be removed with sodium dithionite. The sodium dithionite deprotection is run under mild pH adjustment. As indicated in Bateson et al. at column 3, lines 14-15: "Suitable ester-forming carboxyl-groups are those which may be removed under conventional conditions." Other benzyl protecting groups (such as those of Bateson et al.) are removed with the use of palladium resulting in the need to then remove traces of palladium. This in turn results in a much more difficult process to implement on a larger scale.

Even further, applicants also point out that the use of used p-nitrobenzyl or allyl group in combination with the selected solvent array in accordance with the present invention allows for the isolation of high purity intermediates that result in higher yields when forwarded to the next processing step. This is not the case with the other protecting groups which the Office Action is trying to equate with the p-nitrobenzyl and allyl groups of the present invention.

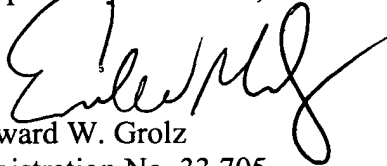
Based on the distinctions between the use of the p-nitrobenzyl and allyl groups in the process of the present invention from the p-methoxybenzyl esters taught by Bateson et al. presented above, it is respectfully requested that the rejection of the claims under 35 U.S.C. §103(a) be withdrawn.

Finally, the Office Action objected to the abstract for allegedly giving "virtually no indication of what the process consists of." Applicants have accordingly replaced the originally filed abstract with a new abstract in which the process of the present invention is more clearly defined. Accordingly, the objection to the abstract is respectfully requested to be withdrawn as well.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned **VERSION WITH MARKINGS TO SHOW CHANGES MADE.**

Based on the amendments and the remarks submitted above, it is respectfully submitted that all the claims in the application contain patentable subject matter and a Notice of Allowance is respectfully solicited.

Respectfully submitted,

  
Edward W. Grolz  
Registration No. 33,705

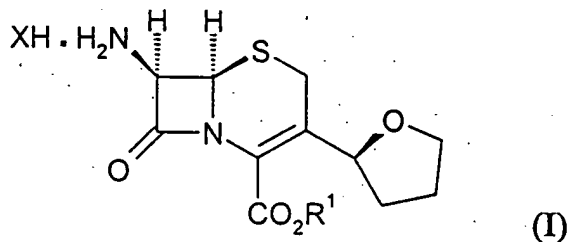
Scully, Scott, Murphy & Presser  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS:**

Please amend claim 1 as follows:

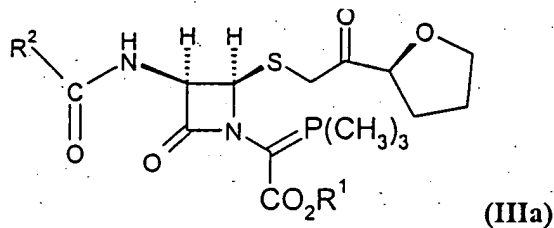
Claim 1 (Amended): A process for preparing a compound of formula (I):



wherein R<sup>1</sup> is para-nitrobenzyl or allyl; and X is halo;

comprising the steps of:

- a) cyclizing a trimethylphosphinic compound of formula (IIIa)



wherein

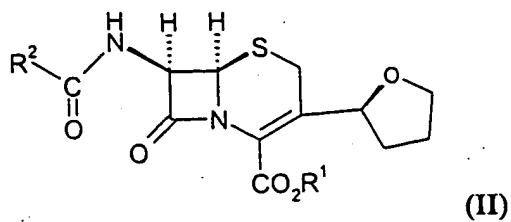
R<sup>1</sup> is para-nitrobenzyl or allyl;

R<sup>2</sup> is selected from the group consisting of C<sub>1-6</sub> alkyl, C<sub>6-10</sub> aryl, C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl

and dithianyl;

in a solvent;

to form a compound of formula (II)



wherein

$R^1$  is para-nitrobenzyl or allyl;

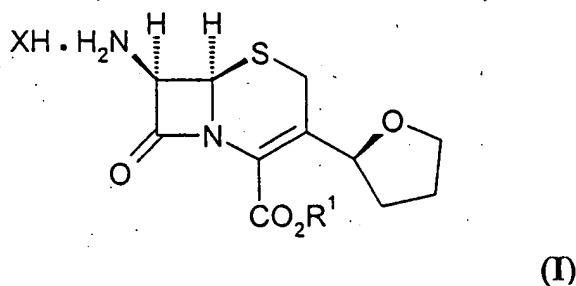
$R^2$  is selected from the group consisting of  $C_{1-6}$  alkyl,  $C_{6-10}$  aryl,  $C_{6-10}$  aryl  $C_{1-6}$  alkyl and dithianyl; and

b) reacting said compound of formula (II) with [an] a Lewis acid of structure  $PX_3$ ,  
where X is a halo group.

**IN THE ABSTRACT:**

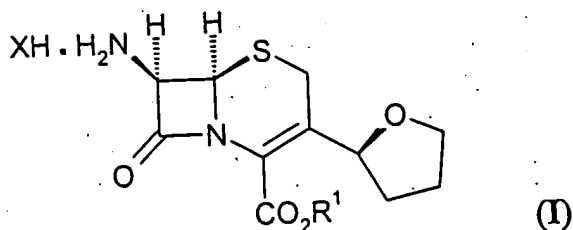
Please replace the Abstract at Page 44, lines 1-8 with new Abstract:

[This invention relates a process for preparing a compound of formula (I)



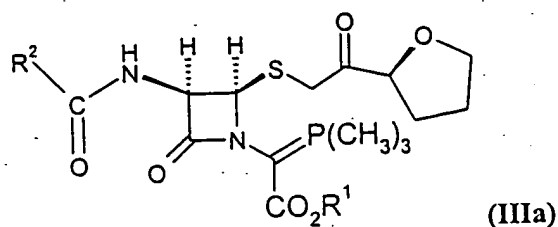
wherein  $R^1$  is para-nitrobenzyl or allyl; and X is halo, which is useful to prepare 3-cyclic-ether-substituted cephalosporins, from trimethylphosphinic compounds]

The present invention relates to a process for preparing a compound of formula (I)

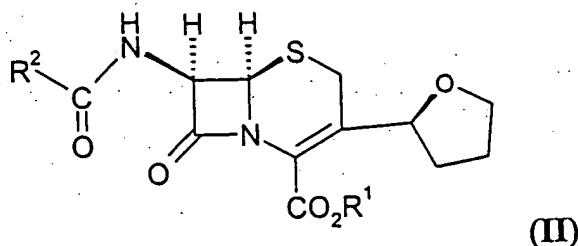


wherein R<sup>1</sup> is para-nitrobenzyl or allyl; preferably para-nitrobenzyl; X is halo selected from the group consisting of bromo, chloro, fluoro and iodo, preferably chloro; by

b) cyclizing a trimethylphosphinic compound of the formula (IIIa):



wherein R<sup>1</sup> is para-nitrobenzyl or allyl, preferably para-nitrobenzyl; and R<sup>2</sup> is selected from the group consisting of C<sub>1-6</sub> alkyl, C<sub>6-10</sub> aryl, C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl and dithianyl; preferably C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl, such as benzyl; in a solvent; to form a compound of formula (II)



wherein R<sup>1</sup> is para-nitrobenzyl or allyl, preferably para-nitrobenzyl; and

R<sup>2</sup> is selected from the group consisting of C<sub>1-6</sub> alkyl, C<sub>6-10</sub> aryl, C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl and dithianyl; preferably C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl, such as benzyl;

[And] and if desired

b) reacting said compound of formula (II) with [an] a Lewis acid of structure  $PX_5$  where X is a halo group to form said compound of formula (I). This invention also relates to compounds useful in such process.